

Acute Generalized Pustular Psoriasis presenting with Erythroderma Associated with Shock and Acute Renal Failure

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Abstract

Acute generalized pustular psoriasis is an uncommon but dangerous form of psoriasis with a systemic presentation. Acute exacerbation, an early picture of acute generalized pustular psoriasis (AGPP), can be fatal, therefore, early recognition and systemic therapy is critical. It is an important differential diagnosis of erythroderma. Epidemiology, etiology, diagnosis, and treatment options are discussed in this paper.

Introduction

Psoriasis is a common skin disease and may manifest with various clinical pictures. Acute generalized pustular psoriasis (AGPP) is recognized as an uncommon form of psoriasis that can be fatal if not treated in a timely manner. Initial clinical presentations may mimic other diseases that presents with erythroderma. Sometimes its clinical picture resembles those of acute generalized exanthematous pustulosis (AGEP). We experienced a patient with a history of psoriasis that initially presented with erythroderma, fever and hypotension. The patient subsequently developed generalized pustulosis and desquamation, which lead us to the diagnosis. Although AGPP may not be common, primary care physicians must be aware of this disease as one of the differential diagnoses of erythroderma.

Case Presentation

A previously healthy 67-year-old man presented with profound fatigue and generalized itchiness on his back. The patient woke up with acute onset of itchiness and redness on his back. Subsequently, he developed chills, tactile fever, diarrhea, light-headedness, tightness of chest, and profound weakness. On examination in the office, the patient had generalized erythroderma and significant orthostatic hypotension and was immediately admitted to the hospital. Past medical history included coronary bypass surgery, appendectomy, peptic ulcer disease, and psoriasis. He took NSAID intermittently for cervical radiculopathy, but denied any allergy to food or medications, recent ingestion of uncooked food, or recent foreign travel.

On examination, the patient was in moderate discomfort with temperature 36.7C, respiratory rate 20/

min, blood pressure 122/60mmHg in supine and 78/48mmHg in standing position, and heart rate 72/min in supine and 84 /min in standing position. There was generalized erythema on his entire body including head, trunk, and extremities without blisters. There were well demarcated scaly round plaques, approximately 4x 2cm on right anterior chest and left upper back. No lymphadenopathy was noted. Heart sounds were normal without murmurs. Lungs were clear bilaterally. Bowel sounds were hyperactive, but there was no tenderness on abdominal palpation. Occult blood was positive. There were several thickened dystrophic toenails without pitting.

Laboratory evaluation revealed hemoglobin 15.4g/dL, WBC count 14.4x10⁹/L with 21% bands. Chemistry abnormalities included BUN 58 mg/dL and creatinine 5.9mg/dL. Urinalysis revealed protein (++) , specific gravity 1.030, sediment 0-5 RBC and 10-12 WBC/hpf; few to moderate bacteria/hpf, and 5 to 10 hyaline and granular cast /lpf. Chest X-ray was unremarkable.

The patient was treated with rigorous fluid replacement for presumed dehydration from recurrent diarrhea and fever. Renal function rapidly improved following rehydration. Toxic Shock Syndrome (TSS) of unknown origin was suspected initially because of the suspicious skin lesions and the patient was started empirically on cefazolin. On the 2nd hospital day, numerous pustules, 2 to 3 mm in diameter, erupted on both flank and thighs (Figure 1). These pustules progressively spread covering 70-80 % of the trunk and 80% of extremities. The lesions became confluent with marked discharge and pooling of subepidermal pus. The Gram stain of the exudates had rare WBC, and the culture did not show significant bacterial organisms. Blood and stool cultures were negative. Despite the systemic antibiotic treatment, he continued to have spiking fever and watery diarrhea. Upon further interview, the patient revealed history of an acute exacerbation of psoriasis treated with methotrexate and prednisone one year prior to this episode. A dermatology consultant recommended starting acitretin

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for possible pustular psoriasis. Soon after the medication started, the affected skin became dry and desquamated and systemic symptoms resolved. The punch biopsy of the lesion showed psoriasis. The patient was discharged on 13th hospital day in stable condition.

Discussion

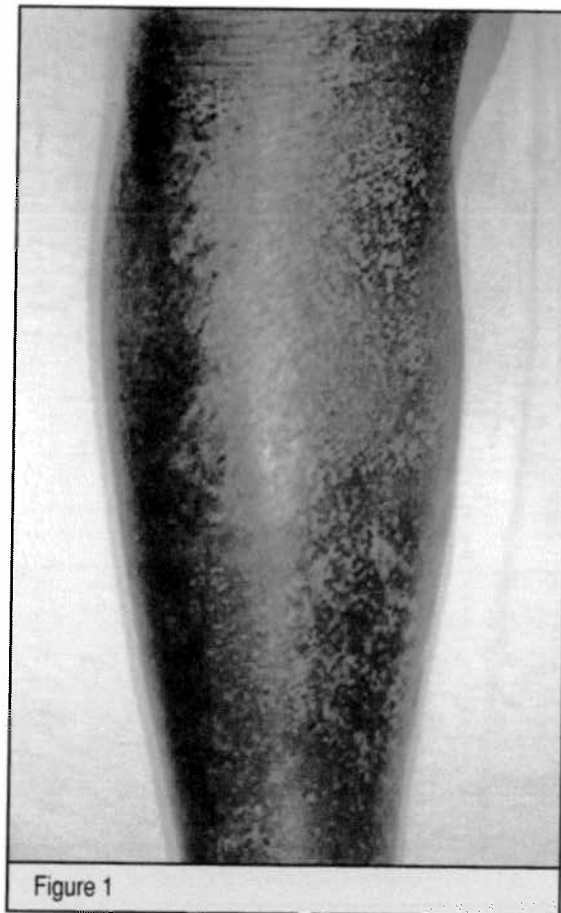
Epidemiology

Psoriasis is a common, chronic, recurrent, inflammatory skin disease and its prevalence is estimated to be approximately 1.0% to 2.0% of people in the US.¹ Its annual incidence was estimated to be 60.4/100,000 (54.4 for men, 60.2 for women).² The incidence varies in ethnic origins; it is low in South American Andes (0%),³ American Samoa (0%),⁴ and high in Norway (4.8%), Denmark (2.9%), and Faroe Island (2.8%). Both sexes are equally predisposed and all age groups are affected. The average age of onset is usually in the 20's, raging from birth to 8th or 9th decade. More females have earlier onset before the age of 30 than males.⁴ Faroe Island series indicated a milder course in later onset (after 25) group. Onset before age 10 is likely to have a more severe course,⁴ although the onset of the disease is less common in the very young and elderly.⁵ The incidence of acute generalized pustular psoriasis (AGPP) is generally much lower but a reliable data is not available.

Clinical manifestations

There are many varieties of lesions, and various descriptive terms have been applied to diverse appearances of psoriasis. The classic form typically presents with well-defined erythematous plaques with sharp borders and silvery gray scaling on the surface. The Koebner phenomenon, precipitated by the trauma, is a well-known lesion. The lesions on hands and feet are generally less erythematous, but well demarcated and have white scales. The lesion on scalp and in skin folds may mimic seborrheic dermatitis although they usually lack typical silver scale. Guttate type is another form of psoriasis, which manifests as small erythematous papules with fine scale, and is frequently generalized and occasionally develops into an explosive eruption of teardrop-shaped lesions primarily on trunk.⁴

As for pustular psoriasis, it can be divided into two groups; non-acute form and acute generalized pustular psoriasis (von Zumbusch; AGPP). The two forms have different mortality rates. The former includes generalized pustular psoriasis of pregnancy, circinate and annular pustular psoriasis, juvenile and infantile pustular psoriasis, and localized form. This entity carries better prognosis.⁴ Typical AGPP starts with erythema and subsequently forms lakes of pus periungually and at the edges of psoriatic plaques. Generalized erythema and more pustules usually follow. Pruritus and intense burning cause extreme discomfort and the patient may be severely ill because of



concomitant constitutional symptoms such as fever, general malaise, arthralgia, and myalgia. The pustules dry up to form yellow-brown crusts over a reddish brown, and shiny surface. In the absence of effective treatment, it can be fatal because of serious complications such as cardiac failure, respiratory failure, hypoalbuminemia, hypocalcemia, acute renal tubular necrosis, and pulmonary embolism due to deep vein thrombosis.¹ Inflammatory polyarthritides is also commonly seen.

Etiology and predisposing factors

The alteration of keratinocyte differentiation such as epidermal hyperproliferation, altered maturation of skin cells, vascular changes and inflammation are associated with the pathogenesis of psoriasis.⁶ But genetic and precipitating factors are more complicated than was previously suspected.⁵ Psoriasis can be induced by many drugs such as beta blockers, lithium, and anti-malaria agents among others. More recent studies revealed terbinafine,⁷ calcium channel blockers, captopril, glyburide, and the lipid-lowering drugs such as gemfibrozil may also induce this condition.¹ Systemic steroids or short-term cyclosporin therapy is well known to cause rebound.⁸

In acute GPP, precipitating factors include strongly irritating topical therapy, pregnancy, sunlight, hypocal-

Table 1.—Differential Diagnoses of Erythroderma

Primary Cutaneous Disorders	
Atopic dermatitis	Contact dermatitis
Fungal diseases	Ichthyosiform dermatoses
Lichen planus	Mycosis fungoides
Pemphigus foliaceus	Photosensitivity reaction
Pityriasis rosea	Pityriasis rubra pilaris
Psoriasis	Pyoderma with reaction
Scabies	Seborrheic dermatitis
Stasis dermatitis	
Systemic Diseases	
Colon carcinoma	HIV infection
Leukemia	CTCL
Lymphoma	Multiple myeloma
Reiter' s syndrome	Sezary syndrome
Systemic lupus erythematosus	Toxic epidermal necrolysis
Staphylococcal scaled skin syndrome	
Drugs	
Sulfonamides and Sulfones	Penicillins
Cephalosporins	Anticonvulsants
NSAID' s	Codeine
Heavy metals	INH
Quinidine	Captopril
Iodine	Antimalarias
Phenothiazines	Methotrexate

alcemia following accidental parathyroidectomy and number of drugs including salicylates, iodine, lithium, phenylbutazone, oxyphenbutazone, trazodone, terbinafine and penicillin as well as withdrawal of cyclosporin treatment.^{4,9-10}

Differential Diagnosis

The clinical manifestations of psoriasis are usually characteristic enough to establish the diagnosis and skin biopsy is not necessary. Histopathologic findings or laboratory tests are not specific and will not establish the diagnosis with certainty. Once it changes its behavior and become eruptive, pustular or erythematous, establishing the diagnosis becomes more difficult.¹¹

This case presented with shock, diarrhea, erythroderma with laboratory data suggestive of deteriorating renal function and bacteremia. This clinical septicemia picture directed us to four possible infectious process. Causes of erythroderma are shown in Table 1. In our case, initially toxic shock syndrome appeared to be most likely until he developed pustulosis on the 2nd hospital day. The differential diagnoses of pustulosis are listed in Table 2. In this case the history of psoriasis may be adequate to make the diagnosis of AGPP. But acute generalized exanthematous pustulosis (AGEP) is also known to have similar clinical picture, which may be difficult to differentiate from AGPP.¹² We concluded this case as AGPP because of the following factors (i) history of psoriasis (ii) good response to acitretin treatment (iii) no known precipitating factors such as medications to cause AGEP (iv) AGEP usually present with more polymorphic lesions including pseudo-erythema and multiform pruritic lesions with associated edema. (v) This case didn't appear to have a self-limiting course until the commencement of acitretin. AGEP should be spontaneously resolving and could have resolved more rapidly.¹³

Although the histological findings obtained from the classic plaque was consistent with psoriasis, it might not reflect overall clinical pictures. We fortunately obtained a timely consult from a dermatologist and the patient had a favorable outcome. Although development of AGPP from classical plaque-type psoriasis vulgaris is rare, this case reminds us to be aware of this life-threatening condition as one of the differential diagnosis of erythroderma.¹⁴

Treatment and outcome

There are several modes of treatment for AGPP. However, choosing appropriate measures is challenging. If the patient is not under immediate life-threatening condition, the initial management should be conservative. But once the patient manifests systemic symptoms, we should consider systemic treatment. The choices of systemic drugs for AGPP include methotrexate (MTX), cyclosporine, and retinoid.¹⁵

Table 2.—Differential Diagnoses of Generalized Pustulosis

Scute generalized pustular psoriasis (AGPP)
Acute generalized exanthematous pustulosis (AGEP)
Acute pemphigus foliaceus
Banai staphylococcal
Banai candidiasis
Pustular eruption due to iodine or bromide
Gram negative or other septicemia

MTX has been the mainstay of treatment for acute GPP since the late '50s. The most dangerous potential side effect is acute myelosuppression especially in the elderly and patients with renal impairment.¹⁶ Cyclosporin is effective for severe plaque-type psoriasis and is also proved to be effective in erythrodermic and generalized pustular psoriasis. It is nephrotoxic, but reversible after drug withdrawal. The combination with PUVA therapy is also reported to have a good response.¹⁷ Retinoids, the derivative of vitamin A and etretinate used formerly, was replaced by acitretin. Its teratogenicity restricts the use for the patients in childbearing age.⁴

Conclusion

We experienced a case with psoriasis, which developed acute generalized pustular psoriasis. Even its clinical picture of initial erythroderma is typical for acute generalized pustular psoriasis, we should consider early consultation of dermatologist and obtaining tissue during acute phase in order to make a definitive diagnosis and ruling out acute generalized exanthematous pustulosis. Early recognition and immediate systemic treatment is critical in AGPP.

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